Chapter 289

Hermansky-Pudlak Syndrome: Case Report

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ABSTRACT
INTRODUCTION: Hermansky-Pudlak syndrome is a rare disease of autosomal recessive origin, with low incidences worldwide (1:1000000), except in Puerto Rico, whose incidence approaches 1:1800. It is composed of oculocutaneous albinism, platelet dysfunction and, in some cases, there is pulmonary fibrosis, insufficiency renal and colitis. The diagnosis is made by the clinic, ophthalmological and platelet count exams, as well as genetic testing to evaluate the prognosis. The treatment is based on a multidisciplinary approach to improve the quality of life since there is still no curative treatment. CASE PRESENTATION: The patient, 2 years old, consulted with a pediatrician to evaluate abdominal pain, diarrhea with blood in the stool, and progressive weight loss for 2 months, also reporting a prolonged episode of epistaxis after local trauma. On physical examination, oculocutaneous albinism and pulmonary auscultation with crackling rales at the base are noted. DISCUSSION: the most suitable optical resource was the Galileo 2.8x telescope. The treatment of granulomatous colitis is done through immunomodulatory therapy, performed in the treatment of Crohn's disease. When the disease becomes refractory to treatment with medications, surgical interventions such as colectomy are performed. CONCLUSION: Because it is a rare syndrome and difficult to diagnose, a better understanding of the pathogenesis of Hermansky syndrome is necessary.

Keywords: Hermansky-Pudlak syndrome, Pediatrics, Case report.

1 INTRODUCTION

Hermansky-Pudlak syndrome (HPS) is a rare disease of autosomal recessive origin discovered in 1959 through two adult patients with severe hemorrhagic diathesis and hypopigmentation who were seen

by Hermansky physicians and Pudlak, which gave the disease its name.[1] To date there are 10 HPS genetic subtypes (1-10) described in the medical literature.

HPS has already been identified in various ethnicities of the world, with a worldwide prevalence of 1 in 500,000 to 1,000,000 in non-Puerto Rican individuals, because due to a specific founding effect, Puerto Rico has the highest estimated prevalence of HPS in 1 in 1800 individuals.[1]

The clinical picture is characterized by oculocutaneous albinism, platelet dysfunction, and in some cases the appearance of pulmonary fibrosis, granulomatous colitis, as well as renal and cardiac disorders.[2] The diagnosis can be made by the clinic of oculocutaneous albinism and hemorrhagic disorder caused by dysfunctional platel, associated with the analysis of platelet electron microscopy and genetic testing that is recommended to determine the specific subtype of the disease.[3]

The treatment needs to be based on the care of a team of specialists with a multidisciplinary approach capable of maintaining the best possible quality of life for the patient since there is still no curative treatment.[1]

2 CASE PRESENTATION

The patient, 2 years old, consulted with a pediatrician to evaluate abdominal pain, diarrhea with blood in the stool, and progressive weight loss for 2 months, also referring to a prolonged episode of epistaxis after local trauma. On physical examination, oculocutaneous albinism and pulmonary auscultation with crackling rales at the base are noted.

3 DISCUSSION

Hermanky-Pudlak Syndrome is an extremely rare disease that was first described in 1959 by 2 Czechoslovak doctors named Hermansky and Pudlak who have since given the syndrome its name .[4] They described two albino adults in the age group of 40 years with increased bleeding time.7

It consists of ten known autosomal recessive disorders (HPS1 to HPS-10).[6] Oculocutaneous albinism is an autosomal recessive disorder. The syndrome is described with a small number of dense platelet granules, these granules are responsible for storing ADP (adenosine diphosphate), and ATP (adenosine triphosphate), which generate the secondary aggregation of platelets, when they are decreased provoke the hemorrhagic change leading the prolonged duration of bleeding time.7

Stores of ceroids are stored mainly in the lungs, gastrointestinal tract, and kidneys.[7] The most feared clinical manifestation is the development of fibrosis pulmonary. Fibros and pulmonary diseases usually present more frequently in patients between 40 and 50 years of age. It is more prevalent in the HPS-1 and HPS-4 subtypes.7 The life expectancy of patients is directly related to the genetic subtype. All patients who have subtype 1 will develop the disease. In the other subtypes, the chance of acquiring fibrosis is variable. Among the gastrointestinal complications, granulomatous colitis is the most common, it presents clinically

in a similar way to Crohn's disease colitis, with irregular involvement of the large intestine, regions of the normal mucosal architecture, crypt abscesses, and infiltration of inflammatory cells into the areas involved.[8]

However, renal dysfunction, colitis, and pulmonary fibrosis are associated with infiltration by deposits of ceroid lysosomes.[9'10'11] It has an incidence of 1 case for each 500,000 to 1,000,000 worldwide. Most patients are in northwestern Puerto Rico in Arecibo-Aguadilla where inbreeding is very common. The frequency found there is from 1 to 1,800.7'[8'12] Women are affected at the same rate as men. Carriers of the syndrome have also been identified in India[13] and the United Kingdom. [14]

The most common and most severe disorder among the 10 subtypes is given by HPS-1 because it has a higher risk mainly of pulmonary fibrosis and is more frequent in the northwestern region of Puerto Rico. Subtypes 2 and 10 are related to chronic neutropenia and recurrent infections. Subtype 3 is found in central Puerto Rico and 4 in Europe.[6'10'1]7 The other subtypes are much rarer and with reduced severity.[4'7]

3.1 CLINICAL PRESENTATION

The classic triad is composed of oculocutaneous albinism, bleeding due to platelet alteration, and complications caused by the accumulation of liposomes in different organs, such as pulmonary fibrosis, renal failure, granulomatous colitis, and decreased neutrophils.7'[16] Patients with oculocutaneous albinism present decreased visual acuity and nystagmus7, in addition to astigmatism and myopia.[17'18'19]

Patients often present with epistaxis, bleeding after surgery, childbirth, and dental treatments. Women may present with menstrual bleeding of greater flow.7 Symptoms of pulmonary fibrosis include non-productive cough and dyspnea on exertion. Physical examination may reveal dry rales initially in the lower lung fields. With the evolution of the disease, patients begin to present hypoxia associated with physical exercise and with progression until it is at rest. Signs and symptoms of granulomatous colitis are colic, abdominal pain, fever, weight loss, bloody diarrhea, and perianal fistula.[8]

3.2 DIAGNOSIS

To establish the diagnosis, every patient with the syndrome needs to have oculocutaneous albinism (OCA) and platelet deficit. Genetic testing is recommended to determine specific subtypes because it is of great importance for prognosis. It is extremely important to perform a complete eye examination. The iris transilumi nation test is carried out with the help of a direct ophthalmoscope. Generally, patients with this syndrome have visual acuity of 20/of 200.[20] For the definitive diagnosis, molecular analysis is required. Currently, there are already tests that can be performed for early diagnosis, still in the prenatal phase, such as amniocentesis and chorionic villus biopsy .[21]

The defect in platelet aggregation can be diagnosed by timing platelet aggregation and comparing it with normality using platelet stimulants such as adenosine, adrenaline.[22] or using fresh platelet-rich plasma, in which it is analyzed through an electron microscope that will show the decrease or absence of dense granules.[23]

The diagnosis of pulmonary fibrosis is confirmed by high-resolution computed tomography of the lungs to allow a close inspection of the pulmonary interstitium. Ground-glass opacities and scars can be found and when the disease is well advanced it can course with the loss of lung volume and bronchiectasis. A lung biopsy is not indicated due to the patient's risk of bleeding.[24]

The differential diagnosis of Hermansky-Pudlak Syndrome should be made with another syndrome called Chediak-Higashi which is diagnosed with oculocutaneous albinism, neutropenia, and natural killer cell dysfunction. For the diagnosis in this case it is necessary the presence of giant granules in the neutrophils.[24]

3.3 TREATMENT

A study conducted with data from 77 albino patients aged 1 to 53 years old at the Benjamin Constant Institute between 2003 and 2014 showed that the most adapted optical feature was the Galileo 2.8x telescope. All patients reported vision gain with the equipment. The optical resources helped in the improvement of the visual function and quality of life of patients with ocular albinism. Strabismus can be treated with optical or surgical measures. Eye protection and early visual stimulation through glasses with special lenses should be used to improve vision and reduce sensitivity to light.[21'27]

It is of utmost importance to prevent burns and skin cancer with the daily use of sunscreen for the skin and lips, and wearing clothes with long sleeves to cover and consequently protect the skin. Have annual checkups with the dermatologist. The hemorrhagic alteration can be treated with blood or platelet transfusion.7

Lately, they are using Desmopressin prophylactically, in addition to activated factor VII, leading to reduced bleeding time. It is necessary not to use aspirin.7 The only effective treatment of pulmonary fibrosis, especially when cases are in advanced stages, is the transplantation of this organ, but recently randomized double-blind studies controlled by Placebos revealed that a drug called Pirfenidone showed a significant decrease in the evolution of fibrosis.7[26'27]

The treatment of granulomatous colitis is done through immunomodulatory therapy, carried out in the treatment of Crohn's disease. When the disease becomes refractory to treatment with medications, surgical interventions such as colectomy are performed.[8]

4 CONCLUSION

Hermansky-Pudlak syndrome is an uncommon autosomal recessive disease that usually occurs at a young age, characterized by skin albinism, platelet dysfunction, and other clinical manifestations associated with the expressive genetic subtype.

The diagnosis consists of the association of the clinic of oculocutaneous albinism and hemorrhagic disorder due to platelet dysfunction, added to the analysis of platelet electron microscopy and genetic testing.

Due to the rarity and chronicity of the disease associated with difficulty in diagnosis, a better understanding of the pathogenesis of Hermansky syndrome is very important.

By identifying these patients, usually with an unfavorable prognosis, it is possible to develop therapies aimed at the knowledge of the syndrome to provide a better quality of life for the patient and a treatment with an appropriate multidisciplinary approach.

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